What is known.

- Postmortem genetic testing for the most common types of Long QT Syndrome (LQTS) in Sudden Infant Death Syndrome (SIDS) cases identifies a non-synonymous (amino acid altering) genetic variant 10-15% of the time.
- Loss-of-function mutations in *KCNH2* underlies type 2 LQTS (LQT2) and is one of the most common forms of LQTS.
- Functional studies show that 95% of LQT2-linked missense mutations have a loss-of-function phenotype in vitro.

What the study adds.

- This study investigates several *KCNH2* missense variants identified in a cohort of ~300 SIDS cases using in vitro (functional studies), in silico (ventricular action potential modeling), and electronic health care record (EHR) analyses.
- The data suggest that the *KCNH2* missense variants are not LQT2-causative variants and therefore do not represent the pathogenic substrate for SIDS in the variant-positive infants.
- The study suggests that there is a minimal role for LQT2-causing mutations in SIDS despite the relatively high frequency of nonsynonymous *KCNH2* variants in SIDS cohorts.

Tweet

The role for missense *KCNH2* varaints that cause short or long QT syndrome in SIDS cases is minimal.